PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Applicant:	Watkins, Jeffry D.	Group Art Unit: 1644	
Serial No.:	10/553,938	Examiner: Ron Schwadron, Ph.D.	
Application Date:	October 21, 2005	Confirmation No.: 8652	
For:	CD20 Binding Molecules		
Docket No.:	X-16760A		

DECLARATION OF APPLICANT UNDER 37 C.F.R. § 1.131

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, David M. Marquis, hereby declare the following:

A duly executed Declaration and Power of Attorney was filed on October 21, 2005 in the above-referenced patent application, declaring that Julian Davies, Jeffry D. Watkins, Barrett W. Allan, Brian Ondek, and myself are the original and first inventors of the subject matter which is claimed and for which a patent is sought in the above-referenced patent application, and the same is true and correct.

I understand that a Business Wire article entitled "Applied Molecular Evolution Advances Optimized Versions of anti-TNF alpha and anti-CD20 Monoclonal Antibody Therapeutic Candidates", dated January 3, 2003 (hereinafter, the "Business Wire reference") has been cited by the Examiner in the above-referenced patent application as anticipating the pending claims of the same.

I have also read and understand the Business Wire reference. In relevant part, the Business Wire reference describes, in entirely functional terms, a CD20 binding antibody,

AME-133, reported to have improved functional attributes as compared to Rituxan®, a therapeutic CD20 binding antibody known and commercialized at the time of the publication of the Business Wire reference.

I also understand that the above-referenced patent application presently claims compositions comprising a CD20 binding molecule (e.g., antibodies or CD20 binding fragment thereof) comprising a set of three structurally defined heavy chain CDRs and a set of three structurally defined light chain CDRs.

The invention presently claimed by the above-referenced patent application was based on detailed experiments involving antibody optimization which resulted in functionally improved CD20 binding antibodies comprising the CDRs defined by specific amino acid sequences.

This declaration is to establish the actual reduction to practice in the United States of the invention claimed in the above-referenced patent application, at a day prior to January 3, 2003, which is the effective date of the Business Wire reference.

At the relevant time of the actual reduction to practice of the invention claimed by the above-referenced application, I held the position of Senior Research Scientist at Applied Molecular Evolution (AME), Inc.

The invention disclosed and claimed in the instant patent application was reduced to practice (in the United States) prior to January 3, 2003, as is evidenced by the attached Exhibits, which are more fully described below.

To the best of my knowledge and belief, the claimed invention was not sold or in public use in the United States for one year prior to the date of the above application.

To the best of my knowledge and belief, the claimed invention was not patented nor described in a printed publication in such a manner that a person of ordinary skill in the field of the invention would have been able to make or use the claimed invention, without undue experimentation, prior to the date of the above application.

This document hereby incorporates the entirety of the concurrently filed affidavit of Jeffrey D. Watkins, dated June 29, 2011, including the exhibits attached thereto.

The exhibits were generated and/or prepared by AME employees, including Christine Hawelka and Ying Nie, who are not inventors of the claimed subject matter, while recording and/or documenting work conducted (in the United States) under the direction and supervision of

myself and/or the other inventors listed on the Declaration and Power of Attorney filed on October 21, 2005.

The following documents are submitted as evidence establishing the date of completion of the claimed invention of the above-referenced application as being prior to January 3, 2003.

a. Copies of sequence files generated with Sequencher™ (Gene Codes Corp.) on October 10, 2002 showing sequences encoding heavy chain variable regions and light chain variable regions of CD20 binding molecules, including those of AME 33 (Exhibits 1-4).
b. Copies of various pages from Christine Hawelka's AME Research Notebook #585, dated from October 9, 2002 to October 17, 2002 (Exhibit 5).
c. Copies of the cover page and page 19 (dated November 4, 2002) from Ying Nie's AME Research Notebook #613 (Exhibit 6).

The documents submitted as Exhibits 1-6 clearly demonstrate that the presently claimed invention was reduced to practice (in the United States) on or before October 10, 2002.

The documents submitted as Exhibits 1-6 clearly demonstrates that the presently claimed invention was reduced to practice (in the United States) prior to January 3, 2003, the effective date of the Business Wire reference.

I further declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code, and that such willfully false statements may jeopardize the validity of this application or any patent issuing thereon.

David M Marquis

David M. Marquis

6-29-11

Date

DESCRIPTION OF THE EXHIBITS

Exhibit 1

A copy of an electronic sequence file generated with Sequencher™ software (Gene Codes Corp.) on October 10, 2002 showing the sequences (both nucleotide and amino acid sequences) obtained from DNA sequencing of the DNA encoding the heavy chain variable regions of various CD20 binding molecules. In particular, the nucleotide sequence encoding the heavy chain variable region of the CD20 binding molecule AME 33 is shown as the fourth nucleotide sequence down from the top of the page (i.e., 1_DM.33.530_F04_12.abl). Directly below the fourth DNA sequence is the amino acid sequence (provided in conventional single-letter code) of the heavy chain variable region of the CD20 binding molecule AME 33.

Exhibit 2

A copy of an electronic sequence file generated with Sequencher™ software (Gene Codes Corp.) on October 10, 2002 showing the sequences (both nucleotide and amino acid sequences) obtained from DNA sequencing of the DNA encoding the light chain variable regions of various CD20 binding molecules. In particular, the nucleotide sequence encoding the light chain variable region of the CD20 binding molecule AME 33 is shown as the fourth nucleotide sequence down from the top of the page (i.e., 1_DM.33.355_F05_11.abl). Directly below the fourth DNA sequence is the amino acid sequence (provided in conventional single-letter code) of the light chain variable region of the CD20 binding molecule AME 33.

Exhibit 3

A marked up version of Exhibit 1 has been provided here as Exhibit 3 for the Examiner's convenience.

The amino acid sequences of CDRH1, 2, and 3 of the CD20 binding molecule AME 33 are underlined at page 2, 3, 4 and 5, respectively, of Exhibit 3. The underlined amino acid sequences of CDRH1, 2, and 3 correspond exactly to SEQ ID NOs: 25, 39, and 57, respectively, of the above-referenced application. Importantly, SEQ ID NOs: 25, 39, and 57 are all recited elements in present claim 34.

Furthermore, in Exhibit 3, the amino acid sequence of the entire heavy chain variable region of the CD20 binding molecule AME 33 has been enclosed by brackets (starting at page 1 and ending at page 5). The entire heavy chain variable region of the CD20 binding molecule AME 33 (shown enclosed in brackets) corresponds exactly to SEQ ID NO: 61 of the above-referenced application. Importantly, SEQ ID NO:61 is a recited element in present claim 48.

Exhibit 4

A marked-up version of Exhibit 2 has been provided here as Exhibit 4 for the Examiner's convenience.

The amino acid sequences of CDRL1, 2, and 3 of the CD20 binding molecule AME 33 are underlined at page 2, 3, and 4, respectively, of Exhibit 4. The underlined amino acid sequences of CDRL1, 2, and 3 correspond exactly to SEQ ID NOs: 5, 13, and 19, respectively, of the above-referenced application. Importantly, SEQ ID NOs: 5, 13, and 19 are all recited elements in present claim 34.

Furthermore, in Exhibit 4, the amino acid sequence of the entire light chain variable region of the CD20 binding molecule AME 33 has been enclosed by brackets (starting at page 1 and ending at page 5). The entire light chain variable region of the CD20 binding molecule AME 33 (shown enclosed in brackets) corresponds exactly to SEQ ID NO:59 of the above-referenced application. Importantly, SEQ ID NO:59 is a recited element in present claim 48.

Exhibit 5

A copy of the cover page, table of contents page, and various other pages from Christine Hawelka's AME Research Notebook #585, dated from October 9, 2002 to October 17, 2002, are provided as Exhibit 5. Throughout these research notebook pages, references to "33", or variations thereof (such as "#33", "33 F1", etc.), are references to the CD20 binding molecule referred to as AME 33 in the above-referenced application.

Page 66 of Christine Hawelka's AME Research Notebook #585, indicates, *inter alia,* that David Marquis ("Dave") set up and finished high-titer ("HT") and ("single-strand") preps of various clones ("31-40"), including clone 33, on October 8, 2002 and October 9, 2002, respectively.

Page 68 of Christine Hawelka's AME Research Notebook #585, describes, *inter alia*, a fixed Ramos cell ELISA binding assay with various CD20 binding molecules, including Fab 33. It is noted on this notebook page, dated October 10, 2002, that "#32, 33, 35, [and] 40 look the best, so will investigate them further". For the avoidance of doubt, the references to "33" or " reference is referred to as AME 33, Fab AME 33 or the like in the present application.

Page 73 of Christine Hawelka's AME Research Notebook #585, indicates, *inter alia*, a fixed Ramos cell ELISA binding assay with various CD20 binding molecules, including the Fab AME 33. The page, dated October 17, 2002, notes that after 18 hours, "Brian's 4H5 as well as 33 [and] 40 staying on pretty well".

Exhibit 6

A copy of the cover page and page 19 Ying Nie's AME Research Notebook #613 are provided as Exhibit 6. Page 19 of Ying Nie's AME Research Notebook #613, dated November 4, 2002, documents the purification of single-strand DNA ("ssDNA") encoding the light chain variable region of clone 33 ("VL33") and the heavy chain variable region of clone 33 ("VH33"). "VL33" and "VH33" on page 19 of this notebook are refer to DNA molecules encoding the light chain variable region and heavy chain variable region, respectively, of the CD20 binding molecule referred to as AME 33 in the above-referenced application.